

REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

By the foregoing amendment, claims 11, 12, 18 and 19 have been canceled without prejudice or disclaimer of the subject matter recited therein. Further, claims 1-7, 13-14, 16-17 and 20-23 have been amended to further clarify the claimed invention. Support for the amendments can be found throughout the specification. In addition, new claims 26-28 have been added. No new matter has been added.

I. Priority

The Examiner has acknowledged Applicants' claim for foreign priority based on Japanese Application No. 146358/1999 filed in Japan on May 26, 1999. However, the Examiner has indicated that a certified copy of the application has not been filed. Applicants hereby submit a certified copy of Japanese Application No. 146358/1999 as required by 35 U.S.C. § 119(b).

II. Drawings

The Examiner has stated that the drawing on page 2 of the specification should not be incorporated in the body of the specification, but instead should be submitted on a separate sheet of paper. Applicants submit that the drawing on page 2 of the specification is not a drawing of the present specification, but instead, the drawing is a depiction of the

results from ^{14}C -tracer experiments reported in *Phytochemistry*, 31:2575 (1992). However, in order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's objection, Applicants have deleted the drawing from page 2 of the specification.

III. Substitute Specification

The Examiner has required a substitute specification in proper idiomatic English and in compliance with 37 C.F.R. § 1.52(a) and (b). Applicants hereby submit a substitute specification as well as a marked-up copy of the specification indicating the amendments to be made via the substitute specification. For clarity and completion, Applicants have also included amendments to the specification from the Amendment and Reply filed on February 6, 2001, already made of record by the Examiner. In particular, a paper copy of the sequence listing (filed on February 6, 2001) has been added after the last page of the substitute specification, currently page 27. Please amend the remaining page numbers accordingly. This substitute specification is in full compliance with the sequence listing rules set forth in 37 C.F.R. §§ 1.821-.825. Applicants submit that no new matter has been added with regard to the substitute specification.

IV. Rejections under 35 U.S.C. § 101

Claims 1-6 and 11-12 have been rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory matter. In order to expedite prosecution in the subject application,

and not to acquiesce to the Examiner's rejection. Applicants have cancelled claims 11-12 and amended claims 1-6 to recite that the DNA or RNA molecule is "isolated."

Therefore, Applicants respectfully request withdrawal of the rejection of claims 1-6 and 11-12 under 35 U.S.C. § 101.

V. Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-2, 4-5, 7, 11-14 and 16-23 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:2 or those encoding SEQ ID NO:1 and plant cells and plants transformed with those nucleic acids, allegedly does not reasonably provide enablement for nucleic acids that encode SEQ ID NO:1, encode modified nucleic acids or that hybridize under unspecified stringency to nucleic acids that encode SEQ ID NO:1. Applicants respectfully traverse this rejection.

Specifically, the Examiner has stated that the specification fails to provide guidance for which amino acids of SEQ ID NO:1 can be altered, which amino acids they can be replaced by, and which amino acids must not be changed to maintain 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase activities of the encoded protein. The Examiner has further stated that the specification fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Applicants submit that the ultimate question is whether the specification contains a sufficiently explicit disclosure to enable one having ordinary skill in the relevant field to

practice the invention claimed therein without the exercise of undue experimentation. *Ex Parte Forman*, 230 U.S.P.Q. 546, 547 (PTO Bd. App. & Int. 1986). (Emphasis added).

It is well within the purview of the skilled artisan to modify nucleotide sequences by deletion, substitution or insertion and then determine if such modified sequences maintain the desired enzymatic activity. Further, it is well within the purview of the skilled artisan to produce modified nucleotide sequences and determine if such modified sequences hybridize to the sequence of SEQ ID NO:1 under stringent conditions. Furthermore, it is well within the purview of the skilled artisan to determine if proteins encoded by these modified nucleic acids maintain the recited enzymatic activities. These types of experimentation are merely routine and do not constitute undue experimentation. The specification need not teach what is known in the art (e.g., modifying nucleic acid sequences). In fact, the Federal Circuit has stated that a patent need not teach, and preferably omits, what is well known in the art. *See Hybritech, Inc. v. Monoclonal Antibodies, Ind.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

Therefore, applicants respectfully request withdrawal of the rejection of claims 1-2, 4-5, 7, 11-14 and 16-23 under 35 U.S.C. § 112, first paragraph.

Claims 18-23 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The Examiner has stated that the claims are broadly drawn to methods for producing any plant secondary metabolite in any plant and for modifying the composition of any plant secondary metabolite in any plant by transformation with a nucleic acid of SEQ ID NO:2, however, the specification only provides guidance for suppression of N-methyltransferase activity in coffee by transformation with an anti-sense construct comprising SEQ ID NO:2. The Examiner has further stated that there was no demonstration that the levels of caffeine or the levels of any other plant secondary metabolite were altered.

In order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have cancelled claims 18-19 and amended claims 20-23 to recite that the plant cell or plant tissue is from a *Camellia* or a *cofea* plant.

Therefore, Applicants respectfully request withdrawal of the rejection of claims 18-23 under 35 U.S.C. § 112, first paragraph.

Claims 1-2, 4-5, 7, 11-14 and 16-23 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner has stated that the claims are broadly drawn to a multitude of DNA molecules, however, the specification only describes a coding sequence from *Camellia sinensis* that comprises SEQ ID NO:2, which encodes a full-length enzyme. Based thereon, the Examiner has stated that Applicant has not described DNA molecules that encode an N-methyltransferase within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Applicants submit that it is well within the purview of the skilled artisan to modify nucleotide sequences by deletion, substitution or insertion and then determine if such modified sequences maintain the desired enzymatic activity. Further, it is well within the purview of the skilled artisan to produce modified nucleotide sequences and determine if such modified sequences hybridize to the sequence of SEQ ID NO:1 under stringent conditions. Furthermore, it is well within the purview of the skilled artisan to determine if proteins encoded by these modified nucleic acids maintain the recited enzymatic activities. These types of experimentation are merely routine and do not constitute undue experimentation. The specification need not teach what is known in the art (e.g., modifying nucleic acid sequences). In fact, the Federal Circuit has stated that a patent need not teach, and preferably omits, what is well known in the art. *See Hybritech, Inc. v. Monoclonal Antibodies, Ind.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986).

Therefore, Applicants respectfully request withdrawal of the rejection of claims 1-2, 4-5, 7, 11-14 and 16-23 under 35 U.S.C. § 112, first paragraph.

VI. Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-7, 11-14 and 16-23 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants respectfully traverse this rejection.

Claim 1, 3, 4 and 6 have been rejected for reciting "of a sequence listing" or "of the sequence listing." In order to expedite prosecution in the subject application, and not to

acquiesce to the Examiner's rejection, Applicants have amended claims 1, 3, 4 and 6 to no longer recite "of a sequence listing" or "of the sequence listing."

Claims 1 and 4 have also been rejected for reciting the phrase "that is a polypeptide having an amino acid sequence of SEQ ID NO:1." The Examiner has suggested replacing the phrase with "of SEQ ID NO:1." In order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have amended claims 1 and 4 to no longer recite "that is a polypeptide having an amino acid sequence of SEQ ID NO:1."

Claims 1 and 4 have also been rejected for not reciting parts (a) and (b) in the alternative. In order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have amended claims 1 and 4 to recite "or" instead of "and."

Claims 1 and 4 have also been rejected for reciting "obtained by carrying out nucleotide replacement, deletion or insertion." The Examiner is not clear as to how many nucleotides or which nucleotides have been replaced, deleted or inserted. Applicants submit that the claims recite that the substitutions, deletions or insertions are made such that the enzyme encoded by the modified nucleic acids maintains the three enzymatic activities. Therefore, one skilled in the art would understand that substitutions, deletions or insertions can be made to the nucleic acids sequence as long as the resulting enzyme retains the recited enzyme activities.

Claims 1 and 4 have also been rejected for reciting "in said nucleotide sequence (a) within a range where a polypeptide encoded by said nucleotide sequence (a) can maintain

said enzyme activities." The Examiner has stated that from the wording of the claim, it appears that the nucleotide sequence is not modified because the claim requires that the polypeptide be encoded by the nucleic acid of part (a) which is not modified. This rejection is rendered moot in light of the amendments to claim 1 and 4. Specifically, claims 1 and 4 have been amended to recite that the modified nucleotide sequence is obtained by carrying out nucleotide replacement, deletion, or insertion in nucleotide sequence (a) such that a polypeptide encoded by said modified sequence maintains the enzyme activities.

Claim 1 has been rejected for reciting "enzyme activities of 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase." The Examiner is not clear as to which enzyme activity (i.e., binding, catalysis, localization, heat denaturation) are being referred to. This rejection is rendered moot in light of the amendments to claim 1. Specifically, claim 1 has been amended to recite that the N-methyl transferase of SEQ ID NO:1 has "the N-methyltransferase enzyme activities of 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase."

Claims 2 and 5 have been rejected for reciting "under stringent conditions." Applicants submit that it is well known in the art what is meant by "stringent hybridization conditions." In particular, stringent hybridization conditions are described in Sambrook et al., Molecular Cloning: A laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press (1989) and Current Protocols in Molecular Biology; Wiley Interscience. However, in order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have amended claims 2 and 5 to recite that hybridization

occurs in hybridization buffer at a temperature ranging from 40° to 80° C for a time period ranging from several hours to overnight. Support for this amendment can be found on page 13 of the specification.

Claims 3 and 6 have been rejected for reciting "a nucleotide sequence of SEQ ID NO:2" and "a nucleotide sequence of SEQ ID NO:3," respectively. The Examiner has stated that it is unclear whether the entire sequence, or just a single nucleotide from that sequence, is intended. This rejection is rendered moot in light of the amendments to claims 3 and 6. Specifically, claims 3 and 6 have been amended to recite "SEQ ID NO:2" and "of SEQ ID NO:3," respectively.

Claim 7 has been rejected for reciting "a constitution for expressing." The Examiner has stated that the term "constitution" is not an art recognized term. This portion of the rejection is rendered moot in light of the amendment to claim 7. Specifically, claim 7 has been amended to recite "a promoter for expressing" instead of "a constitution for expressing." Support for this amendment can be found on page 18, lines 9-22, of the specification.

Claims 11 and 12 have been rejected for reciting the phrase "all or part of." The Examiner has stated that the size of the "part" is unclear. This rejection is rendered moot in light of the cancellation of claims 11 and 12.

Claims 11 and 12 have also been rejected for reciting "wherein the enzyme activities of the plant cells can be inhibited when introduced into plant cells having said enzyme activities." The Examiner has stated that it appears that either enzyme activities or plant

cells are being introduced into plant cells and expressed. This rejection is rendered moot in light of the cancellation of claims 11 and 12.

Claim 13 has been rejected for reciting "A vector comprising a DNA or an RNA molecule as claimed in claim 1." The Examiner has stated that claim 1 is drawn to a DNA molecule, not an RNA molecule, and that vectors do not commonly comprise RNA molecules. In order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have amended claim 13 to recite "A vector comprising a DNA molecule as claimed in claim 1."

Claim 14 has been rejected for reciting "N-methyl transferase having enzyme activities of 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase . . . or having a function of inhibiting the expression of the N-methyl transferase." This portion of the rejection is rendered moot in light of the amendments to claim 14. Specifically, claim 14 has been amended to recite that "the vector encodes N-methyl transferase with 7-methyl xanthine N3 methyl transferase, theobromine N1 methyl transferase, and paraxanthine N3 methyl transferase activities in cells of at least one of microorganisms or plants." Further, claim 14 has been amended to no longer recite "having a function of inhibiting the expression of the N-methyl transferase."

Claim 14 has also been rejected for not being in proper alternative format. The Examiner has stated that the phrase "cells of at least one of microorganisms and plants" should be rewritten in Markush format (i.e., "cells selected from the group consisting of microorganisms and plants") or to replace "and" with "or." This portion of the rejection is

rendered moot in light of the amendment to claim 14. Specifically, claim 14 has been amended to recite "in cells of at least one of microorganisms or plants."

Claims 16-21 and 23 have been rejected for reciting the phrase "plant body." The Examiner has stated that it is unclear what is meant by "plant body" because this term is not an art-recognized term. Applicants submit that the term "plant body" is well defined in the specification. Page 22, lines 11-14, state that the term "plant body" means "the whole individual organism classified into plant or organ parts thereof such as leaves, stems, roots, flowers, fruits, seeds and the likes." However, in order to expedite prosecution in the subject application, and not to acquiesce to the Examiner's rejection, Applicants have amended claims 16, 17, 20, 21 and 23 to recite "whole plant" instead of "plant body" to further clarify the claimed invention.

Claims 19 and 21 have been rejected for reciting "the plant secondary metabolite." The Examiner has stated that there is insufficient antecedent basis. This rejection is rendered moot in light of the cancellation of claim 19 and the amendment to claim 21. Specifically, claim 21 has been amended to recite "a plant secondary metabolite" instead of "the plant secondary metabolite."

Claim 20 has also been rejected for reciting "the plant body" without sufficient antecedent basis. This portion of the rejection is rendered moot in light of the amendments to claim 20. Specifically, claim 20 has been amended to recite "culturing the plant cell or plant tissue as claimed in claim 16 to form a plant body, and culturing said plant body."

Claim 18-21 has been rejected for reciting "the plant cell or plant tissue" without sufficient antecedent basis. Applicants believe the Examiner is in error because there is

sufficient antecedent basis for this phrase in claim 16 (i.e., a plant cell, plant tissue, or plant body).

Claims 18 and 19 have been rejected for reciting "using the plant cell, plant tissue or plant body as claimed in claim 16." The Examiner has stated that claim 16 is not drawn to a method of using a plant cell, plant tissue or plant body. This portion of the rejection is rendered moot in light of the cancellation of claims 18-19.

Claim 20 has been rejected for not reciting "a" before the phrase "plant secondary metabolite." This portion of the rejection is rendered moot in light of the amendment to claim 20. Specifically, claim 20 has been amended to recite "a" before the phrase "plant secondary metabolite."

Claim 23 has been rejected for reciting "Therbroma" instead of "Theobroma." This portion of the rejection is rendered moot in light of the amendments to claim 23. Specifically, claim 23 has been amended to recite "Theobroma" instead of "Therbroma." Applicants submit that the recitation of "Theobroma" was a typographical error.

Claims 18 and 19 have been rejected for not setting forth active, positive steps for the method or process. This portion of the rejection is rendered moot in light of the cancellation of claims 18 and 19.

Claims 18-23 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Specifically, the Examiner has stated that claim 21, for example, ends in culturing a plant cell or tissue or growing a plant body, when the claim should end in the production of a plant with a modified composition of plant secondary metabolite. This

portion of the rejection is rendered moot in light of the cancellation of claims 18-19 and the amendments to claims 20-23.

Therefore, Applicants respectfully request withdrawal of the rejection of claims 1-7, 11-14 and 16-23 under 35 U.S.C. § 112, second paragraph.

VII. Rejections Under 35 U.S.C. § 102

Claims 1-2, 4-5, 7, 11-14 and 16-23 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Stiles et al. (U.S. Patent 6,075,184). Applicants respectfully traverse this rejection.

The Examiner has stated that Stiles et al. teaches an isolated nucleic acid encoding a xanthosine-N7-methyl transferase, and a method of using the nucleic acid to modify caffeine levels in the plant (claims 1-42). Further, the Examiner has stated that this nucleic acid would encode a modified version of SEQ ID NO:1, would hybridize under low stringency conditions, and the protein it encodes would share an "enzyme activity" with it.

It is well settled law that to anticipate a claim, a single reference must teach each and every element of the claim, and the single reference must be enabling. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

The claimed enzyme, which was first found and obtained by Applicants, has three enzyme activities (i.e., 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase activities). Applicants submit that the

nucleotide sequence of claim 1 of the present application is based on the amino acid sequence of SEQ ID NO:1. Part (b) of claim 1 includes modified nucleotide sequences obtained by carrying out nucleotide replacement, deletion, or insertion in SEQ ID NO:1.

Figure 1 of the cited reference shows a metabolic pathway for caffeine synthesis. The cited reference describes only the presence of the compounds in the metabolic pathway in Figure 1 in the tracer experiments. The cited reference does not describe the DNA encoding the enzyme or the enzyme according to the present invention. That is to say, the cited reference describes only a xanthosine-N7-methyl transferase which is not the enzyme according to the invention.

Applicants submit herewith a diagram (Exhibit A) of the metabolic pathway for the biosynthesis of caffeine to show the positions along the pathway where the enzyme activities of the present invention occur. It is clear that the enzyme of the cited reference is involved in the step of caffeine synthesis where xanthosine is converted to 7-methyl xanthosine. See column 2, lines 2-6 and column 6, lines 30-55 of Stiles et al. However, the enzyme of the present invention is involved in three different reactions steps of the caffeine biosynthesis pathway (i.e., 7-methyl xanthine to theobromine (see P1 in Exhibit A); theobromine to caffeine (see P2 in Exhibit A); and paraxanthine to caffeine (see P3 in Exhibit A)).

Further, Applicants submit the following data establishing that the enzyme of the invention does not possess xanthosine-N7-methyl transferase activity.

Substrate	Recombinant Enzyme	Enzyme extracted from tea leaves
7-Methylxanthine	100	100
3-Methylxanthine	1.0	17.6
1-Methylxanthine	12.3	4.2
Theobromine	18.5	26.8
Theophylline	trace	trace
Paraxanthine	230	210
Xanthosine	not detected	not detected

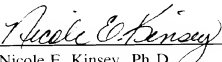
As can be seen, when the enzyme of the present invention, either recombinant or extracted, is in the presences of Xanthosine (the substrate for xanthosine-N7-methyl transferase), no product is detected. Therefore, the enzyme of the present invention does not possess this activity.

Accordingly, because the cited publication does not teach each and every element of the claimed invention, Applicants respectfully request withdrawal of the rejection of claims 1-2, 4-5, 7, 11-14 and 16-23 under 35 U.S.C. § 102(b).

In the event that there are any questions relating to this paper, or the application in general, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Attachment to Amendment dated February 19, 2002
Marked-up Claims

1. (Amended) [A] An isolated DNA molecule comprising any of the following nucleotide sequences:

(a) a nucleotide sequence encoding N-methyl transferase [that is a polypeptide having an amino acid sequence] of SEQ ID NO:1 [of a sequence listing and having enzyme activities of 7-methyl xanthine N3 methyl transferase, theobromine N1 methyl transferase, and paraxanthine N3 methyl transferase; and] and having the N-methyltransferase enzyme activities of 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase; or

(b) a modified nucleotide sequence obtained by carrying out nucleotide replacement, deletion, or insertion in said nucleotide sequence (a) [within a range where a polypeptide encoded by said nucleotide sequence (a) can maintain] where a polypeptide encoded by said modified sequence maintains said enzyme activities.

2. (Amended) The isolated DNA molecule as claimed in claim 1, wherein said nucleotide sequence (a) and said modified nucleotide sequence (b) can be hybridized [under stringent conditions] at a temperature ranging from 40° to 80°C for a time period ranging from several hours to overnight.

3. (Amended) The isolated DNA molecule as claimed in claim 1 or 2, wherein said nucleotide sequence (a) consists of [a nucleotide sequence of] SEQ ID NO:2 [of the sequence listing].

4. (Amended) An isolated RNA molecule comprising any of the following nucleotide sequences:

(a) a nucleotide sequence encoding N-methyl transferase [that is a polypeptide having an amino acid sequence] of SEQ ID NO:1 [of a sequence listing and having enzyme activities of 7-methyl xanthine N3 methyl transferase, theobromine N1 methyl transferase, and paraxanthine N3 methyl transferase; and] and having the N-methyltransferase enzyme activities of 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase; or

(b) a modified nucleotide sequence obtained by carrying out nucleotide replacement, deletion, or insertion in said nucleotide sequence (a) [within a range where a polypeptide encoded by said nucleotide sequence (a) can maintain] where a polypeptide encoded by said modified sequence maintains said enzyme activities.

5. (Amended) [An] The isolated RNA molecule as claimed in claim 4, wherein said nucleotide sequence (a) and said modified nucleotide sequence (b) can be hybridized [under stringent conditions] at a temperature ranging from 40° to 80°C for a time period ranging from several hours to overnight.

6. (Amended) The [An] isolated RNA molecule as claimed in claim 4 or 5, wherein said sequence (a) consists of [a nucleotide sequence of] SEQ ID NO:3 [of the same sequence].

7. (Twice Amended) An expression vector comprising the DNA molecule as claimed in claim 1 and a [constitution] promoter for expressing said N-methyl transferase encoded by the DNA molecule in plant cells.

13. (Twice Amended) A vector comprising a DNA molecule [or an RNA molecule] as claimed in claim 1.

14. (Amended) The vector as claimed in claim 13, wherein the vector [is capable of expressing] encodes N-methyl transferase [having enzyme activities of] with 7-methyl xanthine N3 methyl transferase, theobromine N1 methyl transferase, and paraxanthine N3 methyl transferase activities in cells of at least one of microorganisms [and] or plants [or having a function of inhibiting the expression of the N-methyl transferase].

16. (Amended) A plant cell, plant tissue, or whole plant [body] wherein the plant cell, plant tissue, or whole plant [body] is transformed with the vector as claimed in claim 13 or 14.

17. (Twice Amended) A plant cell, plant tissue, or whole plant [body] as claimed in claim 16, wherein the vector is introduced by infection.

20. (Twice Amended) A method for producing a plant secondary metabolite comprising: culturing the plant cell or plant tissue as claimed in claim 16 [; and growing the plant body] to form a plant body, and culturing said plant body to produce a plant secondary metabolite, wherein said plant cell or plant tissue is a Camellia or a coffea plant cell or plant tissue.

21. (Twice Amended) A method for modifying a composition of [the] a plant secondary metabolite comprising: culturing the plant cell or plant tissue [, or growing plant body] as claimed in claim 16 to form a plant body, and culturing said plant body to modify a composition of a plant secondary metabolite, wherein said plant cell or plant tissue is a Camellia or a coffea plant cell or plant tissue.

22. (Twice Amended) The method as claimed in claim [18] 20, wherein the plant secondary metabolite is at least one or more compounds selected from the group consisting of 7-methyl xanthine, paraxanthine, theobromine, and caffeine.

23. (Twice Amended) A method as claimed in claim [18] 20, wherein a transformed whole plant [body] is a Camellia plant[,] or a Coffea plant[, Cola plant, Ilex plant, Neea plant, Firmiana plant, Paullinia plant, or Therbroma plant body].

Exhibit A

Pathway for the Biosynthesis of Caffeine

